EXHIBIT 3

SUPPLEMENTAL EXPERT REPORT

Depakote Claims
v.
Abbott and AbbVie

By: Linda A. Motyka, Ph.D.
MedTrek®, Inc.

November 15, 2017

1. INTRODUCTION

The documents reviewed for this report are found in Exhibit 1 or referenced within the report. If additional information becomes available, rights are reserved to supplement this report.

2. ANALYSIS & OPINIONS

In my original report, I reserved the right to supplement in the event that additional information became available. (*Report, page 2*). At my deposition on November 6, 2017, I was asked by the Abbott attorney whether I had ever seen various studies that were marked as exhibits. I had not seen these studies, and when I asked the Abbott lawyer if she wanted me to read them, her response was "no." Since the deposition, I have now had an opportunity to review the studies, which were offered as exhibits 26, 28, 30, 34 and 35 to my deposition, and based on my review of the studies, particularly with respect to the 2004 label at issue in the Sansone case (Marthee Sansone Depakote dose >1000 mg/day; VPA levels > 70 μg/mL, *see Sansone medical records*), I offer the following opinions in addition to those expressed in my original report, as well as those I testified to in my deposition.

Based on the available studies and data in existence at the time, Abbott knew or should have known, at the latest in the early to mid 1990's, that all AEDs (antiepileptic drugs), including Depakote, carried a significant increased risk for malformations in offspring, such as the type of skeletal abnormality suffered by Anthony Sansone— malformation of the skull and other malformations (including metopic craniosynostosis, marked microcephaly, and mild-moderate developmental delay/ global developmental delay). As such, in addition to the deficiencies I have already expressed regarding the 2004 label, it is further misleading and inadequate because it fails to warn physicians and patients of the risk of malformations. The label fails to warn physicians and patients that VPA (Depakote) is one of the most teratogenic of all the AEDs. The label fails to warn physicians and patients that the teratogenicity of VPA is dose dependent, with a statistically significant occurrence of malformations and doses of VPA and that there was a cut-off value in VPA dose (1000 mg/day) and level (70 μg/mL) for the occurrence of malformations in offspring exposed. It is noted that Marthee Sansone had a previously born healthy child when Marthee Sansone was taking Depakote at doses < 1000 mg/day and VPA levels were < 70 μg/mL to treat her epilepsy (*see Sansone medical records)*.

C. Dravet et al (1992) conducted a prospective study of teratogenic effects of antiepileptic drugs (AEDs) in pregnant women in southeast France, comparing malformation rates with those collected by a birth defects registry. The authors concluded that valproate (VPA) and phenytoin were the most teratogenic (all malformations). REF 1.

S. Kaneko and T. Kondo (1995) summarized the incidence, mechanisms and prevention of birth defects and maternal use of antiepileptic drugs. From prospective studies a number of primary risk factors for increased incidences of congenital malformations in the offspring of epileptic mothers receiving AEDs were identified. These risk factors included high drug dose, high serum drug concentration, the use of AEDs with high teratogenicity potency [primidone > valproic acid > phenytoin > carbamazepine > phenobarbital (phenobarbitone)] and AED polypharmacy (especially combinations of valproic acid and carbamazepine, and phenytoin and/or carbamazepine with or without barbiturates). The authors stated that the use of a controlled release form of valproic acid may helpful in decreasing valproic acid teratogenicity, since the peak concentration of valproic acid and its toxic metabolite is greatly reduced compared with conventional preparations of valproic acid. REF 2.

E. B. Samren et al (1997) quantified the risks of intrauterine antiepileptic drug (AED) exposure in monotherapy and polytherapy by conducting a reanalysis of 5 prospective European studies totaling 1379 children. This reanalysis showed that VPA was consistently associated with an increased risk of MCA (Major Congenital Abnormalities) in offspring born to mothers with epilepsy. The MCA in the study included craniosynostosis and microcephaly in offspring of mothers receiving VPA during pregnancy. The most pronounced increase of risk of MCA was that for children exposed in utero to VPA or CBZ (carbamazepine). The authors also concluded that the risk associated with VPA monotherapy was dose dependent and that the offspring of mothers treated with >1000 mg/day VPA were at increased risk, in particular of neural tube defects. REF 3.

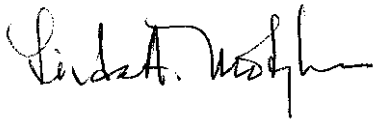
S. Kaneko et al (1999) prospectively analyzed 983 children born in Japan, Italy and Canada to identify the major risk factors for the increased incidence of congenital malformations in offspring of mothers being treated for epilepsy with antiepileptic drugs (AEDs) during pregnancy and to determine the relative teratogenic risk of AEDs. The highest incidence of congenital malformations in children exposed to a single AED occurred with primidone (14.3%), followed by VPA (11.1%), phenytoin (9.1%), carbamazepine (5.7%), phenobarbital (5.1%). The analysis of all AED exposed offspring revealed that there were significant associations between occurrence of malformations and doses of VPA ($P = 0.026$). The results indicated the increased incidence of malformations was caused primarily by AEDs, suggesting that malformations can be prevented by improvements in drug regimen, and by avoiding polypharmacy and high levels of VPA (more than 70 μg/mL) in the treatment of epileptic women of childbearing age. There was a cut-off value in VPA dose (1000 mg/day) and level (70 μg/mL) for the occurrence of malformations in offspring exposed to a single AED while there was no such value in the remaining AEDs in the monopharmacy as well as the polypharmacy groups. The authors stated that with regard to VPA dose and levels, these can be a good clinical guideline

for AED treatment of women with epilepsy of childbearing age. REF 4.

Additionally, there is evidence that Abbott knew or should have known of the risks of developmental delays and cognitive impairment in children born to mothers using Depakote during pregnancy. Meador (2002, ref 39) noted that "a recent retrospective study from England raises questions that another AED might pose special cognitive risks." (Reference to Adab, 2001 study) Meador noted the risk of special education needs appears to be elevated for valproate. REF 5.

N. Adab, et al (2001), retrospectively reviewed a survey of 594 school-age children born to epileptic women, and found that there was a relationship between the use of valproate, either monotherapy or polytherapy, and the increased risks of additional educational needs. The use of valproate during pregnancy poses a special threat to cognitive development of children exposed in utero. REF 6.

Likewise, J. Dean, et al (2002), used a retrospective study to investigate the frequency of neonatal and later childhood morbidity in children exposed to antiepileptic drugs in utero. Among the findings, the rate of developmental delay following valproate exposure at children over 21 months of age was particularly high at 37%. REF 7.



Linda A. Motyka, Ph.D. November 15, 2017

ADDITIONAL DOCUMENTS REVIEWED

1. C. Dravet et al, Epilepsy, antiepileptic drugs, and malformations in children of women with epilepsy: a French prospective cohort study, Neurology 1992; 42 (suppl 5): 75-82.
2. S. Kaneko and T. Kondo, Antiepileptic Agents and Birth Defects, Incidence, Mechanisms and Prevention, CNS Drugs 3 (1): 41-56, 1995.
3. E. B. Samren et al, Maternal Use of Antiepileptic Drugs and the Risk of Major Congenital Malformations: A Joint European Prospective Study of Human Teratogenesis Associated with Maternal Epilepsy, Epilepsia, 38(9): 981-990, 1997.
4. S. Kaneko et al, Congenital malformations due to antiepileptic drugs, Epilepsy Research, 33: 145-158, 1999.
5. K. Meador, Neurodevelopmental Effects of Antiepileptic Drugs, Current Neurology and Neuroscience Reports, 4: 373-378, 2002.
6. N Adab, A Jacoby, D Smith, D Chadwick. Additional educational needs in children born to mothers with epilepsy, J Neurol Neurosurg 2001; 70; 15-21.
7. J C S Dean, H Hailey, S J Moore, D J Lloyd, P D Turnpenny, J Little, Long term health and neurodevelopment in children exposed to antiepileptic drugs before birth, J Med Genet 2002; 39; 251-259.
8. Medical Records of Sansone (Marthee and Anthony)